SEQUENCE LISTING

The patent application contains a lengthy "Sequence Listing" section. A copy of the "Sequence Listing" is available in electronic form from the USPTO web site (http://seqdata.uspto.gov/?pageRequest=docDetail&DocID=US20140068797A1). An electronic copy of the "Sequence Listing" will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

What is claimed is:

1. A DNA-targeting RNA comprising:

(i) a first segment comprising a nucleotide sequence that is complementary to a sequence in a target DNA; and

(ii) a second segment that interacts with a site-directed modifying polypeptide.

2. The DNA-targeting RNA of claim **1**, wherein the first segment comprises 8 nucleotides that have 100% complementarity to a sequence in the target DNA.

3. The DNA-targeting RNA of claim **1**, wherein the second segment comprises a nucleotide sequence with at least 60% identity over a stretch of at least 8 contiguous nucleotides to any one of the nucleotide sequences set forth in SEQ ID NOs:563-682, or a complement thereof.

4. The DNA-targeting RNA of claim **1**, wherein the second segment comprises a nucleotide sequence with at least 60% identity over a stretch of at least 8 contiguous nucleotides to any one of the nucleotide sequences set forth in SEQ ID NOs:431-562, or a complement thereof.

5. The DNA-targeting RNA of claim **1**, wherein the site-directed modifying polypeptide comprises an amino acid sequence having at least about 75% amino acid sequence identity to amino acids 7-166 or 731-1003 of the Cas9/Csn1 amino acid sequence depicted in FIG. **3**, or to the corresponding portions in any of the amino acid sequences set forth as SEQ ID NOs:1-256 and 795-1346.

6. A DNA polynucleotide comprising a nucleotide sequence that encodes the DNA-targeting RNA of claim **1**.

7. A recombinant expression vector comprising the DNA polynucleotide of claim **6**.

8. The recombinant expression vector of claim **7**, wherein the nucleotide sequence encoding the DNA-targeting RNA is operably linked to a promoter.

9. The recombinant expression vector of claim **8**, wherein the promoter is an inducible promoter.

10. The recombinant expression vector of claim **7**, wherein the nucleotide sequence encoding the DNA-targeting RNA of claim **1** further comprises a multiple cloning site.

11. An in vitro genetically modified host cell comprising the DNA polynucleotide of claim **6**.

12. A recombinant expression vector comprising:

(i) a nucleotide sequence encoding a DNA-targeting RNA, wherein the DNA-targeting RNA comprises:

(a) a first segment comprising a nucleotide sequence that is complementary to a sequence in a target DNA; and

(b) a second segment that interacts with a site-directed modifying polypeptide; and

(ii) a nucleotide sequence encoding the site-directed modifying polypeptide comprising:

(a) an RNA-binding portion that interacts with the DNA-targeting RNA; and

(b) an activity portion that exhibits site-directed enzymatic activity, wherein the site of enzymatic activity is determined by the DNA-targeting RNA.

13. A recombinant expression vector comprising:

(i) a nucleotide sequence encoding a DNA-targeting RNA, wherein the DNA-targeting RNA comprises:

(a) a first segment comprising a nucleotide sequence that is complementary to a sequence in a target DNA; and

(b) a second segment that interacts with a site-directed modifying polypeptide; and

(ii) a nucleotide sequence encoding the site-directed modifying polypeptide, wherein the site-directed modifying polypeptide comprises:

(a) an RNA-binding portion that interacts with the DNA-targeting RNA; and

(b) an activity portion that modulates transcription within the target DNA, wherein the site of modulated transcription within the target DNA is determined by the DNA-targeting RNA.

14. A variant site-directed modifying polypeptide comprising:

(i) an RNA-binding portion that interacts with a DNA-targeting RNA, wherein the DNA-targeting RNA comprises a nucleotide sequence that is complementary to a sequence in a target DNA; and

(ii) an activity portion that exhibits reduced site-directed enzymatic activity, wherein the site of enzymatic activity is determined by the DNA-targeting RNA.

15. The variant site-directed modifying polypeptide of claim **14**, comprising an H840A mutation of the *S. pyogenes* sequence SEQ ID NO:8 or the corresponding mutation in any of the amino acid sequences set forth as SEQ ID NOs:1-256 and 795-1346.

16. The variant site-directed modifying polypeptide of claim **14**, comprising a D10A mutation of the *S. pyogenes* sequence SEQ ID NO:8 or the corresponding mutation in any of the amino acid sequences set forth as SEQ ID NOs:1-256 and 795-1346.

17. The variant site-directed modifying polypeptide of claim **14**, comprising both (i) a D10A mutation of the *S. pyogenes* sequence SEQ ID NO:8 or the corresponding mutation in any of the amino acid sequences set forth as SEQ ID NOs:1-256 and 795-1346; and (ii) an H840A mutation of the *S. pyogenes* sequence SEQ ID NO:8 or the corresponding mutation in any of the amino acid sequences set forth as SEQ ID NOs:1-256 and 795-1346.

18. A chimeric site-directed modifying polypeptide comprising:

(i) an RNA-binding portion that interacts with a DNA-targeting RNA, wherein the DNA-targeting RNA com-